# Center for the Evaluation of Risks to Human Reproduction Review Process

The National Toxicology Program (NTP) Center for the Evaluation of Risks to Human Reproduction (CERHR) was established in 1998 to serve as an environmental health resource to the public and regulatory and health agencies. CERHR publishes monographs that assess the evidence that environmental chemicals, physical substances, or mixtures (collectively referred to as "substances") cause adverse effects on reproduction and development and provide opinion on whether these substances are hazardous for humans. A schematic of the review process is provided in Figure 1.

## Selection of Candidate Substances

CERHR invites the nomination of substances for evaluation by anyone at anytime. Nominations may be submitted to NTP at *http://ntp.niehs.nih.gov/* (select "Provide Input to NTP") or to CERHR by mail, fax or via the website (*http://cerhr.niehs.nih.gov/nominate/index.html*).[1] Nominations should contain a rationale or reason for the proposed evaluation and, if possible, appropriate background information and relevant data (*e.g.*, personal concern, journal articles, exposure information, etc.) to support the rationale.

The multi-agency CERHR Core Committee[2] considers each nominated substance to determine whether the available scientific information justifies its formal evaluation. The Core Committee bases its recommendations for evaluation on a substance's production volume, potential human exposure, amount of available scientific information about a substance's reproductive and developmental toxicity, and degree of public concern. Those nominations accepted for evaluation proceed through the review process as discussed below. A nomination might not be selected for evaluation for several reasons, including (1) insufficient scientific information to evaluate whether the substance is a reproductive or developmental toxicant, (2) existence of a recent evaluation of reproductive and development risks conducted by another agency or organization, (3) absent or limited information on human exposures, or (4) insufficient public health concern.

The CERHR announces the substances proposed for evaluation and solicits public comments on them through announcements in the Federal Register and NTP publications. These announcements also invite the submission of new data and information about planned or ongoing studies, exposure, and patterns of use. In addition, CERHR invites

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[2] The Core Committee is an advisory body consisting of scientists from government agencies. Agencies currently represented are: Environmental Protection Agency, Centers for Disease Control and Prevention, Food and Drug Administration, Consumer Product Safety Commission, National Institute for Occupational Safety and Health, and National Institute for Environmental Health Sciences

the public to identify scientists qualified to serve on an expert panel for each specific evaluation. The NTP Board of Scientific Counselors (BSC) then reviews the proposed substances. The public is provided with another opportunity to comment on the proposed evaluations at the public BSC meeting. Circumstances may arise in which a letter review is conducted with a subset of BSC members and/or ad hoc members as needed. The CERHR considers this input to select and prioritize candidate substances for evaluation. The CERHR may defer or terminate the evaluation of a proposed nomination at any time if relevant information becomes available that warrants CERHR reconsidering the substance's evaluation. In such cases, the NTP Board of Scientific Counselors, the NTP Executive Committee[3], and the public would be notified of this action.

**Preparation of Expert Panel Reports**

*Expert Panels*

CERHR convenes an expert panel for each substance selected for evaluation. The expert panel prepares a report ("expert panel report") that (1) reviews the relevant literature for the substance (discussed below) and (2) provides conclusions on whether exposure to the substance could result in adverse effects on human reproduction and/or development. The expert panel is an *ad hoc* group of scientists with relevant expertise and knowledge selected by the NTP in accordance with the Federal Advisory Committee Act and Health and Human Services guidelines and regulations. Panelists are selected primarily from the CERHR Expert Registry, a database maintained by CERHR that contains the names of scientists with expertise relevant to CERHR evaluations who are willing to serve on expert panels. The public may nominate scientists to the CERHR Expert Registry at any time. The CERHR also accepts self-nominations.

*Draft Expert Panel Report*

As a first step in preparation of a report, CERHR staff prepares a literature review for each substance selected for evaluation. This literature review is then disseminated to the expert panel members who, with support of the CERHR staff, prepare a draft expert panel report that includes 4 sections: (1) chemistry, use, and human exposure, (2) general toxicology and biological effects, (3) developmental toxicity data, and (4) reproductive toxicity data. The draft expert panel report provides a basis for writing section 5 (summary, conclusions, and critical data needs) at the expert panel meeting.

After the draft expert panel report is completed, CERHR publishes a Federal Register notice to announce the expert panel meeting and the panel's membership, request public comments on the draft expert panel report (sections 1–4), and invite the submission of written public comments and/or the presentation of oral public comments at the meeting. The draft expert panel report is made available electronically on the CERHR website (*http://cerhr.niehs.nih.gov/*) or in hardcopy by mail from CERHR and its availability is announced through the NTP listserv.[4] An expert panel meeting will generally be held 7

[3] The NTP Executive Committee is composed of the heads (or their designees) of federal research and regulatory agencies and provides advice to the NTP on policy issues.

[4] The NTP listserv is an email distribution list used to disseminate information on NTP activities. To subscribe to the NTP listserv visit *http://ntp.niehs.nih.gov* see "Contact Us."

or 8 weeks after announcement of the availability of the draft expert panel report. All comments received within the period for public comment are distributed to the expert panel for consideration, become part of the public record, and are posted on the CERHR website.

*Expert Panel Meeting*
At the public meeting, the expert panelists (1) revise the draft expert panel report as necessary, (2) reach consensus scientific judgments on the levels of human exposure to the substance and on the potential for these exposures to result in adverse effects on human reproductive and/or development, and (3) identify scientific uncertainties and critical data needs associated with the evaluation (Section 5 of the final expert panel report). The conclusions in the final expert panel report are solely a product of the expert panel. Following the expert panel meeting and completion of the expert panel report, the CERHR posts the report on its website, announces its availability, and requests public comments on the report in a Federal Register notice and through the NTP listserv.

**Preparation of NTP-CERHR Monograph and Transmittal**

Following the public comment period on the final expert panel report, CERHR staff prepares the NTP-CERHR Monograph. The monograph begins with the NTP Brief and includes three appendices. The first appendix lists the expert panel members, the second appendix is the final expert panel report, and the third appendix contains all public comments on the final expert panel report received by CERHR. The NTP Brief provides:

- background information on the substance(s)
- findings of the expert panel
- discussion of any relevant data available after the expert panel meeting
- NTP's conclusions on the potential for the substance to cause adverse reproductive and/or developmental effects in exposed humans

In preparing a draft NTP Brief, the NTP considers all public comments and any additional scientific information available following completion of the expert panel's deliberations and report. In addition, the NTP distributes the draft NTP Brief to the CERHR Core Committee for review and comment. The CERHR then posts the draft NTP Brief on its website, announces its availability, and requests public comments on the document in a Federal Register notice. In addition to the NTP Brief the NTP-CERHR Monograph includes three appendices.

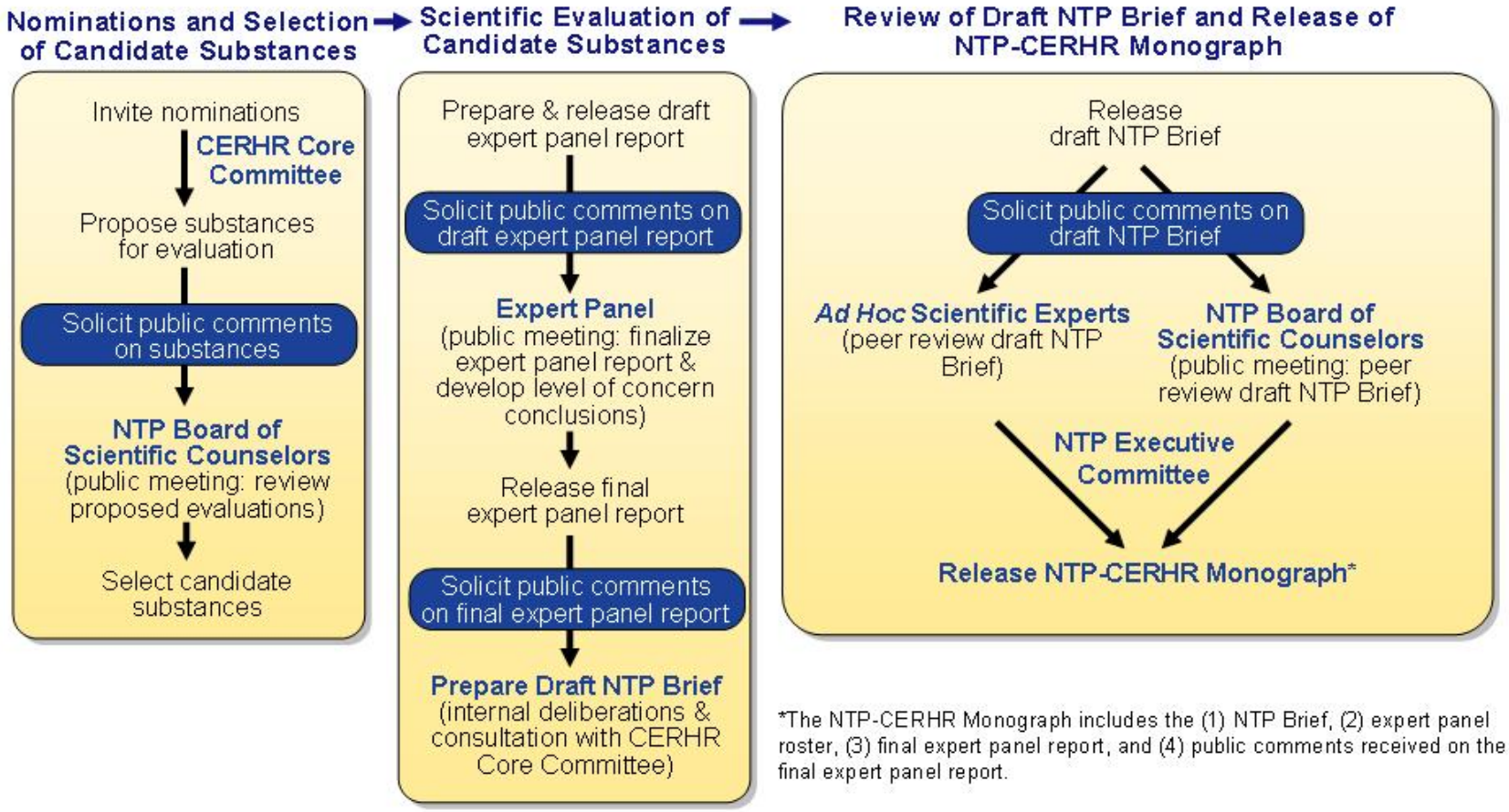
The NTP will use one of two mechanisms for peer review of the draft NTP Briefs. In most instances, the NTP will conduct the peer review through a letter mechanism by 3-5 external, independent, scientific experts. The NTP makes available to the experts all relevant information related to each NTP Brief including the final expert panel report and all public comments received on that report and on the draft NTP Brief. The experts are charged to determine whether the scientific information discussed in the draft NTP Brief supports the NTP's conclusions regarding the potential for the substance to cause

adverse reproductive and/or developmental effects in exposed humans. The peer review comments from the experts are compiled into a peer review report that is posted on the NTP website. In other incidences, for example, where the NTP classifies the Draft NTP Brief as a highly influential scientific assessment[5] the NTP will have the NTP Board of Scientific Counselors (BSC) conduct the peer review at a public meeting with opportunity for public comment. The NTP announces the peer review in the Federal Register and invites the submission of written and/or oral public comments on the draft NTP Brief at the meeting. All public comments received within this time period become part of the public record of the meeting and are posted on the NTP website (*http://ntp.niehs.nih.gov/* see "Advisory Boards & Committees"). The background materials provided to the BSC and their charge will be the same as described above for the letter peer review. Following the meeting, the NTP posts the peer review report on its website.

The NTP makes revisions to the draft NTP Brief, as appropriate, distributes the final NTP Brief to the NTP Executive Committee for review and consultation, and prepares the final NTP-CERHR Monograph that is transmitted to federal and state agencies and disseminated to the public. Availability of the final NTP-CERHR Monograph is announced through the NTP listserv. The NTP disseminates CERHR Monographs free-of-charge electronically on the CERHR website (*http://cerhr.niehs.nih.gov*) and in hard copy or CD from CERHR.

[5]Office of Management and Budget Final Information Quality Bulletin for Peer Review (*http://www.whitehouse.gov/omb/inforeg/infopoltech.html* )

## Figure 1. Center for the Evaluation of Risks to Human Reproduction (CERHR) Evaluation Process




*The NTP-CERHR Monograph includes the (1) NTP Brief, (2) expert panel roster, (3) final expert panel report, and (4) public comments received on the final expert panel report.